5-1-1938

Gas gangrene

Harold H. Macumber
University of Nebraska Medical Center

GAS GANGRENE

BY

HAROLD H. MACUMBER

***

SENIOR THESIS

PRESENTED TO

THE COLLEGE OF MEDICINE

UNIVERSITY OF NEBRASKA

OMAHA, 1938

CONTENTS

INTRODUCTION

Modern surgery has known no greater problem than the successful management of cases of gangrene induced by gas-producing bacilli. No other disease that falls to the lot of the surgeon places so heavy a burden on his judgement nor is so dependent upon his management as this dread condition.

The history of the literature bearing on this subject is a long one, made up, as is the history of most diseases, of a vast number of irrelevant papers, many case reports of value in the final summation, and a few path-forming papers. That there is no completely satisfactory treatment is at once evident by the fact that so many different methods have been propounded. Many more authors could have been quoted, but in the main, it would have been just a repetition of the information already set forth. To keep astride the ever changing viewpoints and the voluminous literature on this subject has been difficult for the average physician. As an assimilation of the literature as well as a general review of the subject to date, this paper is presented.

We define gas gangrene as an infectious form of gangrene, produced by the pathogenic gas-producing bacilli, occurring characteristically in grossly contaminated wounds, and being characterized by certain objective and subjective findings. In this review I have attempted to deal only with the common form occurring in the extremity. Following the various procedures I have attempted to arrive at the most modern and most widely accepted conception of this disease process at the present time.

EARLY HISTORY

Hippocrates, writing of a case of gangrene, although it is not clear that it was of the emphysematous type, said, "Critin of Thasa commenced to experience pain in his foot, in his great toe. He went to bed the same day. He had a slight chill, some nausea, and then a little fever; he became delirious during the night. On the second day there was swelling of the entire foot and of the ankle, which was a little red and tender; there were present tiny black blebs, and he had a great fever. The sick one was entirely out of his head; he died the second day." (73). Celsus is thought by some to have known of the occurrence of gas gangrene in pregnancy for in his chapter on the extraction of the dead fetus we find, "It may so happen that the child may be distended with a humor, from which there flows a fluid with a fetid odor." (109).

Following these early writings there is a long period during which the disease does not seem to have been recognized. Avicenna, Guy de Chauliac, J de Vigo, and Ambrose Pare do not refer to it (73). But in Fabricus de Hilden's works (Opera Omnia, Frankfort, 1776) we find mention of the condition. "It is my belief," he says, "That the principle cause of this terrible ill is some venous humor which Nature has driven into these people." (73).

Quesnay, in 1745, in a chapter on "Gangrene of putrid dissolution of the humoral mass," gave Peyronnie the credit for being the first to describe and furnish exact observations of gas gangrene, and spoke of the "subcutaneous emphysema, the erysipelatous color

of the skin, and the rapidity of death" (73). We find that De la Motte, in 1771, published two observations which have been accepted by some as being cases of gas gangrene (73). In 1786, Thomas Kirkland knew it and called it gangrene of the "emphysematous type" (73).

Early in the Napoleonic Wars, during the nineteenth century, Larrey seemed to have known this disease. In some of his observations he spoke of the rapid progress of traumatic gangrene, which in a few hours spread from the limb and was often fatal in less than ten hours (73). Boyer, in 1814, mentioned its occurrence in fractures and also spoke of the rapidity of death, while Velpeau, in 1829, stressed it as a complication of fractured limbs and considered the emphysema of grave importance (35). In his experience, death was the outcome in most cases. Dupuytren, in his lectures under the name of "spontaneous emphysema," described a condition occurring in trauma resulting in rapid decomposition, and in 1836, we find Martin de Bazas publishing a case of "foudryant gangrene" which followed a crushed foot and in which death occurred in twelve hours (73).

Malgaigne recalls a case of rapid termination after emphysema complicating a fractured limb. He looked for the real cause. "I think," he said, "That there occurs under the influence of shock and stupor a special change which attacks life just as excessive cold will kill the sperm in an egg" (73). For the first time the gas escaping from the emphysema was analyzed, and was found to be

inflammable as well as showing the presence of Hydrogen Sulfide. Renault and Chauveau were among the first to create gangrene in animals (73).

At the meeting of the Academy of Sciences on Oct. 11, 1849, Chassaignac asserted that certain gangrenes with emphysema should be considered as having "a poison far in excess of the mechanical injury." He described four cases the next year which showed what he called "empoissonnement traumatique" (73). Maissonneuve, to whom is often mistakenly given the credit for the first clinical description, reported to the Academy at a later date (Sept. 12, 1853) two cases of gas gangrene and delcared that there existed a certain variety of traumatic gangrene to which he gave the name of "gangrene foudroyante" in which, first, putrefying gas developed in the interior of veins during life; and second, that this gas circulated in the blood and caused a fatal poisoning. Later, in developing the doctrine of "pneumohaematuria" he considered this as a variety of septicemia (69).

During the Crimean War, Pirogoff with the Russian, and Salleron with the Allied Forces, both noted this condition and wrote about it (107). Pirogoff spoke of it as "primary nephritic gangrene," while Salleron reviewed 65 cases collected from the casualties of that War. Dolbeau emphasized the idea that the "autoinfection" was always fatal, and declared himself strongly in favor of immediate amputation (73). Billroth busied himself

for a time with it, and considered the cause to be a decomposition of the mortified elements occurring in the disease. Gurlt discussed it in his book on bone surgery (1862) (73). Bottini is given credit for being the first to demonstrate the infective nature and transmissibility of gas gangrene (112).

In the American Civil War, there is no record of gas gangrene as such. In fact Keen, who served as a military surgeon, stated that he never saw a case (53). It was, however, observed in the Franco-Prussian War. Wyatt observed it at the seige of Paris (73), and Frery mentioned it as occurring in Belfort. Passow declared that it was discussed at a meeting of the German military surgeons in Orleans (73). In his excellent monograph on this subject, Trifaud has collected 123 cases occurring in civil life previous to 1883 (73).

In 1887, Jurgensen described a case, and attributed the gas to a gas forming microbe (112). With the appearance of the "Bacteriological Era," the organisms found associated with the disease were investigated by many workers. Pasteur discovered the Vibrion Septique (78), Koch the bacillus of malignant edema (73), and Welch the gas bacillus (Bacillus Welchi) (114). He was unable to demonstrate spore formation in the early cultures, but this was noted by Fraenkel who also described the Welch bacillus the following year (32).

The clinical aspect of the disease was investigated and

described by Stolz in 1902 (112), Stewart in 1905 (98), Cramp in 1912 (17), and Simonds in 1915 (97).

During the World War great interest was aroused in this disease and the literature which appeared during the years 1914-1919 was enormous. Among a great number of fine papers, perhaps the most comprehensive were the Surgeon General's Report (84) and the Report of the Medical Council of Great Britain (85).

INCIDENCE

While a study of the available statistics leaves one with the impression that gas gangrene has been comparatively rare in civil life, it became of extreme importance during the World War. The multitude of grossly contaminated wounds, occurring in the trenches amid extensively manured soil, served as an ideal type of injury in producing the infection.

In Trifaud's monograph on the subject, he has listed 123 cases occurring in civil life before 1883 (73). In 1900, Welch was able to collect 46 proven cases of gas bacillus infection. Sixteen cases were observed in Baltimore, sixteen others were recorded by other American observers, and only 14 were reported abroad (114). Cramp, in 1912, found 187 cases in the literature, and reported 25 cases from the wards of Belevue Hospital during an eight year period (27). Weintrob and Messeloff, in 1927, reported 85 gas bacillus infections treated in the Belevue Hospital from 1911 - 1926. There were 618,105 admissions during this period, or one case for every 7,310 total admissions (110).

Boland reports that in the Grady Hospital in Atlanta, Georgia, during the seven year period ending in 1929, eighty compound fractures were encountered in Negroes, with 19% developing gas gangrene. During the same period, of 97 cases of similar injuries occurring in white people, only 7% developed gangrene. He brings up the question of whether or not the Negro is not more susceptible to the infection (94).

Millar, in 1932, collected 607 cases of gas gangrene occurring in civil life, exclusive of obstetrical infections. Only those subsequent to the Lister Era were taken. Males were affected six times more frequently than females. The third decade of life furnished the greatest number of cases. Cases were reported from all parts of the world, and no seasonal variation was apparent. This, as well as the above reviews, leaves the impression that gas gangrene is rarely seen in civil practice (73). It must be remembered that there are many more cases occurring throughout the world than are recorded in the literature. Also any one series is perhaps not a fair cross section because of the human tendency to report the bizarre and unusual cases.

Stone and Holsinger reviewed 67 cases occurring at the University of Virginia Hospital from 1921 - 1933. In this series gas gangrene represented an average of 1/1035 hospital admissions, which seems to be rather high. Of interest was the greatly increased incidence since 1926, which they attribute to an increasing number of traffic accidents, the more general use of machinery in the South, and increased industry; all of these would favor production of injuries which are prone to develop gas bacillus infections (99).

As regards military incidence, Gross has published a rather extensive anlaysis covering the years 1916-1917. He states that during the early part of 1916 he passed 2,796 wounded men through his ambulance with 3.6% developing gas gangrene, while during the

latter part of the same year he passed 1,676 men with 1.9% developing the infection (43). Emery, however, emphasized the small percentage of gas bacillus contaminated wounds which developed clinical symptoms (27). Mairesse and Regnier state that they examined 1,016 wounded men bacteriologically, and found only 297 showing contamination with the gas bacillus (66). Sieru and Mercier reported fewer than 0.5% of their wounded developed clinical gas gangrene (96).

Pettit reported a rather complete summary gathered from the Transportable Hospital #8 during the Great War. Of 4,377 patients that were wounded in action during the latter part of 1918, 5.0% developed gas gangrene. This is a rather high incidence, but it should be noted that this hospital received only those seriously wounded. Gas gangrene was a most important cause of death, accounting for 17.0% of all deaths. Of 890 wounds examined bacteriologically, 53% were found to contain anaerobic bacilli; it is an interesting fact, however, that of this number, only 34% at any time developed clinical evidence of gas infection. It is thus seen that in their experience, at least, over two thirds of the wounds contaminated with anaerobes did not develop gangrene (80).

The American Expeditionary Force in France had 1.08% of all wounds of the soft parts develop gas gangrene, according to the Surgeon General's Office (84). The official British Expeditionary Force report gives an incidence of 1.0%. The number of cases

varied in the big pushes, and when it was not possible to treat the wounded quickly, it was of course much higher (85).

ETIOLOGY

We have seen that Fabricus de Hilden mentioned gas gangrene in 1776, and stated that in his opinion the principle cause was a venous humor which "Nature had driven into these people" (41). Malgaigne, in 1839, in attempting to determine the real cause, stated that there occurred under the influence of shock and stupor a special change which attacks life just as excessive cold would kill the sperm in an egg (73).

During the next few years, numerous accounts appeared in the literature concerning cases in which gas wasfound in the vessels at autopsy, and various explanations were advanced to cover these. In Maissonneuve's classical description of the clinical syndrome in 1853, he believed that putrifying gas developed in the veins during life and circulated in the blood, causing a fatal poisoning. Later, in developing the doctrine of "pneumohematuria" he considered this as a variety of septicemia (73). Billfoth considered the cause to be a decomposition of the mortified elements occurring in the disease. (73).

May, in 1857, reported three cases in which air was found in the vessels post mortem. One of these seems to represent a very clear case of typical gas gangrene, occurring in a man who injured his toe. At autopsy, several hours later, air wasfound in the vessels, heart, liver, and subcutaneously in the leg. He attempted to determine the probable source of the gas, and raised the question of whether or not air can enter the circulation during life as well

as whether air could be generated in the body. He concluded that air could enter the veins from a local pathological condition and cause death. Little did he realize just how close to the truth of the matter he actually was (70). One year later he again reported two similar cases, and again seemed to be concerned over the possibility of air being generated in the body during life. (69).

Greene, in 1887, reviewed eighteen such cases in the literature, and concluded that air could and did enter the circulation during surgical operations, deliveries, etc., and caused death (41). The discussion turned generally around the question whether the gas was atmospheric air or the result of putrefaction. This question in most cases could only be solved by bacteriological examination, and efforts began to be directed along this line.

In 1891, Levy isolated a bacillus from a gaseous phlegmon of the pelvis and thigh of a puerperal woman. This organism was anaerobic, gas-producing, non-motile, short, small, delicate, stained by Gram, grew in long threads and chains of thirty or more, and formed Anthrax-like colonies. No experiments upon animals were made (112). In a subsequent article in 1895, Levy declared that this bacillus was identical with Fraenkel's bacillus phlegmonous emphysematosae (112).

Welch and Nuttall, in 1892, reported their classical discovery of the bacillus which they termed Bacillus Aerogenes Capsulatus,

but which is now known as Bacillus Welchi. This occurred in a man with a substernal aeneurysm with recurring rupture. At autopsy the entire body was found to be markedly emphysematous. The blood was found to be rich in bacilli, and extensive bacteriological studies were made. The organism was also injected into laboratory animals and the same post moretm findings were obtained, with recovery of the organism. These men therefore concluded that the organism was the cause of the condition, and called attention to the large number of reported cases of similar autopsy findings in the literature in which no cause could be found. The bacillus was isolated in pure culture and its morphological and biological aspects were extensively studied. They stated that there could be no doubt that the gas found in the vessels and organs at autopsy was not atmospheric air, but was produced by the bacillus. Further, they concluded that the organisms had entered the body through the anaerysmal sac through the external openings on the anterior chest wall. They also stated that in their opinion, the entrance of the gas and bacilli into the circulation was concerned with the death of the patient, however they expressed themselves with reserve on this point. (114).

The first observations of the bacillus aerogenes capsulatus following the report of Welch and Nuttall were made by E. Fraenkel, who published, in January, 1893, a preliminary report, and later in the same year a monograph concerning gaseous phlegmons. Fraenkel

makes no mention of the previous discovery of the same organism by these two men, and evidently was unacquainted with their work. To Fraenkel belongs the credit for the demonstration of the causal relationship of this bacillus to the affection called, at that time, gaseous phlegmon, emphysematous cellulitis or gangrene, gangrene gazeuse, etc. He reported the results of his investigations of four cases of gaseous phlegmon. Two of the cases followed subcutaneous injection of drugs, however in none of these cases was gas found at autopsy in the vessels or organs. The bacillus isolated by Fraenkel corresponded in every way as regards morphological and cultural characteristics with the bacillus aerogenes capsulatus, and to it Fraenkel gave the name bacillus phlegmons emphysematosae. (32).

The probable identity of Fraenkel's bacillus of gaseous phlegmon with the bacillus of Welchi was recognized by Mann, in an article published in 1894. He isolated the bacillus from a case of gas gangrene resulting from a finger injury, and stated that the organism was capable of growing in the living body with the production of gas gangrene without the entry of the gas into the blood vessels. This is the first reported case which recovered after the nature of the infection had been established. (67).

The next publications concerning the bacillus aerogenes capsulatus were those of Graham, Stewart, and Baldwin in 1893. They reported a case occurring following an abortion, in which at autopsy

enormous, generalized emphysema was found. This case was recognized before the autopsy as probably referable to the bacillus described by Welch and Nuttall. The significance of this case is that it afforded positive evidence that the gas bacillus might invade the blood and produce gas widely distributed over the body during life. Bacteriological studies identified the organism as the bacillus aerogenes capsulatus (39).

In 1896, Flexner and Welchi published an extensive paper covering 23 human cases with various pathological manifestations of their bacillus (113), and 1900 Welch published another study of the same nature (112). In this report he states "While it has been demonstrated that various bacteria may be concerned in producing gaseous gangrene, it is now evident that the bacillus that I discovered in 1891 is the one whose causative agency is best established."

The bacillus of malignant edema was first discovered by Pasteur in 1876 after infecting animals with putrid flesh. He termed this the Vibrion Septique, and classified it among his 'septicemie' (78). Several years later Koch found the same bacillus in the human body, and gave the name of bacillus of malignant edema to it (112).

Gwyn, in 1899, reported a case report, which, although it at no time presented symptoms of gas gangrene, nevertheless gave positive blood cultures for the presence of a bacillus which he states he identified as the bacillus of Welch. He concluded that the organism was one of attenuated virulence, and that it was apparently held

in check by the body during life. This was the first case in which the organism was cultivated from the circulation during life (44). Hare, in the same year, reviewed 22 cases with nine deaths (45).

Kausch, in 1915, stated that in his opinion the condition was due to Fraenkel's bacillus alone (52), however Selter, in the same year, examined 14 cases by means of direct smear and culture, and concluded that gas gangrene was not always caused by this bacillus, but might be produced by other anaerobic organisms (95). Jordan, one year later, stated that "While other organisms have been identified with gas gangrene, they are all very similar to the Welch bacillus and may be referred to collectively as "gas bacillus" (107).

Weinberg published a rather extensive review of the bacteriology in 1916, and stated that B. Welchi was very commonly found in the condition, while the Vibrion Septique was found in 4% of the cases only. He produced the infection experimentally in Guinea Pigs and showed that trauma to the muscles and vascular embarrassment were of great importance in its production (108). It was about this time that the literature appears to be literally flooded with articles dealing with this condition. The infection of wounds by gas producing organisms was by no means new; as I have shown, attention had been repeatedly called to infections in previous wars which had resulted in an emphysematous condition of the body. In

the World War, however, the nature of the battle ground, the concentration of large numbers of individuals, and the underground methods of warfare all combined to accentuate the presence of this infection and caused it to assume a prominent role in military surgery.

The Welch bacillus had been long known as a gas producing organism, capable of infecting wounds. Until the outbreak of the World War, surgeons and bacteriologists had not had sufficient experience to justify a positive opinion, as regards the etiological relationship of this and other gas producing organisms, in the production of what had been called gas gangrene. The reason for this reservation had been due largely to the fact that numerous other organisms had been recorded as accompanying an infection of this kind. In addition to this, chains of cocci organisms had been thought at times to have been able to assume a gas-producing role. Among other bacilli found to be present in gangrenous tissues were the colon, proteus, and other putrefactive bacilli. For several months after the World War began the unidentified gas producing bacilli, resembling the Welch bacillus, were known as bacillus perfringens, largely on account of certain cultural characteristics of the Welch bacillus. However as time went on and the bacteriological technic of war hospital laboratories became more perfected, it became apparent to careful observers that the perfringens was really a strain of the Welch organism.

Bull and Pritchett were the first to demonstrate a true exotoxin in B. Welchi cultures. This work was published in 1917, and they showed that the toxin was specific, thermolabile, and antogenic. They also stated that the toxin was a complex of a hemolysin and another poisonous body producing inflammation and necrosis of subcutaneous tissue and muscle (13). In a later publication these same men attempted to determine whether or not one toxin was common to all strains of B. Welchi. They concluded that in the 22 different strains that they had investigated, all had a similar toxin (14).

In 1919, Fasiani referred to an article by Conradi and Bieling in 1916, in which they stated that the different anaerobic bacilli did not constitute different and distinct strains, but rather that they were transformation stages of one species only. Fasiani expressed the opinion that this conclusion was erroneous, and that the various bacilli did constitute different species (28).

Henry, in 1923, emphasized that the toxin of Bacillus Welchi was actually a myotoxin (47). Gemmell, called attention to the possibility of communicating the disease by fomites, and pointed out that the spores resisted ordinary hospital sterilization (37). A year later he stated that in his experience, those cases in which the Vibrion Septique predominated greatly offered a much graver prognosis (37).

Gage, in 1932, called attention to the almost constant

presence of the Welch bacillus in wool cloth and on shot gun wads. He demonstrated that he was able to produce the infection by inserting some of this material into traumatized muscle (36).

Krymov pointed out that the bacillus possessed the ability of lying latent in the tissues for as long as 15 years before initiating clinical signs of the infection, and reviewed several cases of alleged nature (58).

Finesilver stated that, although the Welch bacillus was commonly present, the possibility of a symbiosis is certain, other organisms being Pasteru's Vibrion Septique, B. edemateins, B. histolyticus, and B sordelli. (31).

Touraine, in 1936, emphasized the possibility of the infection's following hypodermic injection. At that time he had collected 83 such cases (102).

At the present time the recognized group of organisms consists of about 25 anaerobes and 15 aerobes. These bacteria have a wide distribution in nature. The organisms usually concerned in gas bacillus infections are as follows:

(1) Bacillus Welchi (B. perfringens, B. aerogenes capsulatus) is the greatest producer of gas and is most often isolated in gas gangrene. It may be found alone, but is usually associated with other organisms. Aerobic saprofytes seem to incite greater pathogenicity. It attacks muscle with avidity, as a result, as many have suggested, of the glycogen. Vincent found this organism in

82% of gas gangrene infections during the war (105).

(2) Vibrion Septique is a rather rare, slender, motile, sporing organism which also produces a classic form of gangrene. It produces less gas but more edema, and therefore predominates in edematous lesions. Most bacteriologists feel that its pathogenicity is anything but feeble. The clinical manifestations of this bacillus begin several days later than B. Welchi and seem to be more superficial. This organism is found in 10% of gas gangrene infections according to Vincent (105).

(3) B. Edematiens is pleomorphic and may resemble Vibrion Septique, B. Sporogenes, and B. Tetani. Its toxin produces a special white edema which more or less masks the gas infiltration. Vincent and Stodel state that this organism is found in from 4-5% of cases of gas gangrene (105).

(4) Bacillus Sporogenes is a common anaerobic associate with the same morphological characteristics as Vibrion Septique, but it is considered to be non-pathogenic. It is motile and is responsible for the putrid character of the wound.

Since these organisms are so widely distributed, the question naturally arises as to why one does not see more of these infections. The answer is probably found in the experiments of Teissier, who demonstrated that gas forming organisms in themselves have but little power to attack the tissues, but, when associated with other organisms, they rapidly produce the typical picture (18). Inoculation with

either B perfringens or B edematiens produces a hard edema which slowly disappears. When growths of aerobic bacteria are added to these cultures, a severe infection results, and the animal rapidly dies. Vincent has shown that, if one injects separately into two Guinea Pigs attenuated B. Welchi and Vibrion Septique, neither alone will produce the gangrene. But if one injects the mixture of either of these with B. sporogenes, a typical gas gangrene will result (105).

PATHOLOGY

Emrys-Roberts and Cowell have presented a very comprehensive summary of the local pathological changes (27). They have divided their discussion into the macroscopic and the microscopic changes occurring; (1) at the wound surface, (2) in the area of dead muscle, (3) at the spreading edge, and (4) in the contractile part beyond.

As regards the macroscopic changes at the wound surface, they state that in the early cases the damaged and infected muscle fibers may be seen to be pale in color and non-contractile, while the wound surface is covered with a thin film of a viscid greenish-yellow fluid. On close examination fine pink lines, indicating the spread of infection into the muscle, run along the course of the perifascicular connective tissue. In the more superficial wounds, the surface is at first a dusky red, later becoming paler, then green, and finally black. This is due to the local contusion producing interstitial hemorrhages, the blood from which is immediately attacked by the products of the bacteriological growth. There is no actual pus exuded from the wound surface, although a thin, clear, foul smelling fluid does escape. Underneath the infective process continues to develop, softening occurs. The surface becomes crepitant to the finger, and soon reaches the final stage of black deliquescence. Microscopically the superficial, obviously necrotic, muscle will be found to be composed of distorted, swollen, fragmented fibers, in whose meshes are large numbers of polymorphoaerobic organisms and cell debris. The vessels are

quickly damaged and thrombosis takes place. The entire mass is effectively bound in a fibrinous reticulum, which, by binding the pieces of dead muscle and the leucocytes, prevents the formation of typical pus, and accounts for its absence in gas gangrene.

In the area of dead muscle in the very earliest cases, if the muscle is examined immediately below the wound surface macroscopically, it is found to be firmer than normal and no longer contractile. There is no change in its color, but there is a distinct lack of luster and translucency. Soon, however, the sequence of color changes appears. The normal red is lightened and becomes pink, thereafter running through the greys and greens to the final black. Gas production begins at a variable time after the death of the muscle, usually it does not occur until many hours have elapsed, so that it must be regarded as a late manifestation. At first minute bubbles are found, these coalesce and rapidly increase in size, giving the dead muscle a spongy appearance. As gas is produced in greater quantities, it forces its way along the planes of least resistance; in this way the fascial sheaths become distended with gas and a mechanical ischaemia is produced from the blood supply being obstructed. This accelerates the spread of gangrene. Massive thrombosis, apart from those resulting from the trauma, are not a concomitant of the typical process of gas gangrene. Microscopically the muscle fibers themselves have lost all normal characteristics of striation and

staining properties. They are swollen, distorted, and fragmented, present longitudinal splitting, and are separated from the surrounding interstitial tissue by distinct spaces. Myolysis frequently proceeds to such a degree as to lead to entire disappearance of the portions of fibers involved. Many of these fibers are in process of active phagocytosis. The leucocytes decrease rapidly in number as we proceed in the direction of the spreading edge, as do also the bacteria. All stages from vessels with normal walls on the one hand, and vessels whose walls have been completely lysed on the other, can be seen.

In advancing cases, as we proceed to the spreading edge of the infection, a point is at last reached where non-contractility ceases, and the muscle again reacts to stimuli. This line of junction is found to extend across the muscle in an extremely irregular fashion, at times being demonstrated at some distance - often several mm - in front of the dead muscle fibers just described. This is possibly the most interesting area of all. Here the proportion of dead to living fibers is reversed, and we find an occasional dead or dying fiber among many living ones. At the spreading edge there is no indication at all of the vascular change in those cases in which the effect of the original trauma can be ruled out. The demonstration, histologically, of the bacilli is very difficult here, but they are known to exist there because their presence can be demonstrated by means of

cultures taken from this area. The soluble toxins of the bacilli exist in the perifibrillar space and are here absorbed by the muscle fibers. Traveling in the direction of the long axis, they kill the fiber as they advance. Heavy bacterial infection, combined with inefficient drainage at the surface, leads to increased absorption of the toxins, and so hastens the advancing death of the individual fibers. Similarly, the more damaged the tissues and the greater the degree of blood extravasation and thrombosis, the less the resistance there is to the lethal process. Hence the astonishing rapidity of the advance in certain cases, more especially if, in addition to the local loss of resistance, we have a lower general resistance resulting from fatigue, shock, and hemorrhage.

Lastly, we can examine the contractile part in advance of the spreading edge. In the absence of traumatic bruising effects, vascular lesions have never been encountered. It must be remembered that traumatic interstitial hemorrhage is quite commonly met with at a considerable distance from the wound. No other sign of macroscopic pathology can be found here. Microscopically, we find a continued development of the fibrinous leucocytic layer, in such a manner as to form a distinct line of demarcation between this layer and the underlying normal muscle. There is usually a sudden transition from the infiltrated layer to the healthy muscle; while within the layer of fibrinous exudate the muscle fibers, where

recovery is taking place, are found to be dead and in the process of phagocytosis. The perifibrillar and perifascicular spaces contain the anaerobic toxins which by reason of their antichemiotactic properties repel leucocytes. We are, therefore, justified in saying that the greater the mass of leucocytic aggregation, the better the defense is proceeding. Later, when the stage of recovery is still further advanced, the fibrinous exudate with dead muscle, is shed in the form of sloughs; revealing, beneath, the establishment of true granulation tissue, with loops of capillaries being formed and remains of muscle fibers undergoing absorption. This is a sign that the underlying tissues have regained their vital properties. Leucocytes, no longer bound in the messes of the fibrinous reticulum, are freely permitted to return to the tissues and to be shed as pus. Regeneration of such a highly specialized tissue as muscle fiber must necessarily be of a very imperfect nature, and many investigators question the possibility of any real replacement of lost muscle tissue (75, 20).

Kausch, in 1915, described three forms; the mild, in which the infection is largely limited to the subcutaneous tissue, the severe, in which muscle involvement predominates, and the fulminating, in which all local tissues are concerned alike (52). Albrecht, 1916, reported that in his opinion death was due largely to a direct action of the toxin upon the heart. He also maintained that in many acute cases that there was an acute failure of the Adrenal,

and stated that in such cases he had found a decrease in lipoid substance in the Adrenal (1).

Adrenal depression, as evidenced by a diminution of lipoid substance in histological section, was again referred to by later workers (15,104,5,64).

Wallace, in 1917, studied the color changes occurring in the muscle and skin. He reported that the area first became a pale color due to the swelling, which was followed by a dirty cream tint which established that gangrene was present. Areas of purple staining now appear, which rapidly enlarge and coalesce, followed by blebs which are filled with a blood stained fluid. The purple color then becomes a deep greenish yellow which is the final stage (106). These findings were confirmed by Emrys-Roberts and Cowell (27).

McNee and Dunn, in 1917, stated that the rapidity of spread of gas gangrene into living muscle required an explanation by a different process than that which governs ordinary septic invasion of tissues. They suggested that the sheaths inclosing the fibers, being easily detachable, form potential spaces into which the toxic material can readily pass, causing necrosis of the fiber (71). This was again confirmed by later workers (27).

Taylor believes that the chief agent at work is the evolved gas which by its mechanical pressure inhibits the blood supply, devitalizes the tissues, fragments the muscle, and scatters the

infection (101). If it is true, however, that gas production, except in the fulminating type, is a late stage of gas gangrene, then it can not be regarded as the chief factor. This view, as I have stated above is taken by Emrys-Roberts and Cowell (27).

Razzaboni gives complete autopsy reports on a series of cases. He states that the heart is pale, flacid, and dilated, especially the auricles. Microscopically the heart shows a separation of the muscle fibers. The lungs commonly present hypostatic congestion with foci of bronchial pneumonia, while histologically hyperemia and interstitial hemorrhage are seen. The thyroid gland is negative. The kidneys, stomach and bowel are hyperemic. The liver is enlarged and hyperemic, while on section it presents a diffuse fatty degeneration with multiple foci of inflammatory infiltration. The changes in the spleen are characterized by vasodilatation and hyperplasia of the malpighian corpuscles. The adrenals are intensely hyperemic and often hemorrhagic. The retroperitoneal nodes are hyperplastic (82).

Bingold states that in his opinion the bacteremia is one of the chief contributing causes of death (5).

CLINICAL PICTURE

The symptoms and signs arising from limited foci of infection with anaerobic bacilli are in keeping with the pathological changes outlined above. The disease occurs a variable time after the reception of a wound, particularly if this is lacerated and associated with much trauma and hemorrhage into the tissues, or with the fracture of a bone. Loss of blood leading to shock, as well as any previous disease tending to impair the blood supply to the part (diabetes, arterial disease) act as predisposing factors and greatly aggravate the picture.

Emrys-Roberts and Cowell consider three main clinical types in their discussion of the symptomatology of gas gangrene infections (27):

(1) The common type which occurs in neglected wounds 12-24 hours after the injury,

(2) The fulminating type, where the patient, especially if untreated, may be dead in a few hours,

(3) The delayed type, with a slow onset so that the condition only becomes established several days, weeks, or even months after the injury.

(A) THE COMMON TYPE: One of the earliest symptoms is pain coming on about 36-48 hours after the original injury, and becoming rapidly more severe. A marked rapid rise of pulse rate about the same time is to be expected. Such a combination of symptoms should lead one to examine carefully the injured part. The area does not

have the physical characteristics of a pyogenic abscess; there is no redness or increased skin temperature. The skin overlying the lesion is exceedingly tender with alternating anemic and discolored redish black patches. The discharge from the wound is not purulent, but an irritating brownish watery fluid with a sickly foul odor. Later as the edema increases and the gas develops, it becomes dusky and bronzed in appearance. Wallace has carefully studied these changes in the color of the overlying skin, and feels that they are of great importance in the following the progress of the pathology (106). The systemic signs accompanying such an infection afford a strong contrast with those of other types of localized infection. I have mentioned the very rapid and easily compressible pulse; there is an alarming fall of blood pressure, and all the signs of complete collapse are noted. Respiration becomes rapid and shallow, and the patient runs a moderate fever, usually from 100 - 103 F. Vomiting is a distressing feature at times, and in the last stages may become black from petechial hemorrhages. Mentally these patients are often perfectly clear, and it is not uncommon to see a man smoking a cigarette or reading a newspaper a few hours before death. Mild delirium is noted at times but is not common. Later, as true gangrene sets in, the tissues become a dirty green and black color. The presence of gas cannot be detected in the early stages, and must always be considered as a late phenomena. The best means of detecting its

early presence is by stroking with a flat instrument, which gives a distinctly crepitant note. The bubling of gas from the wound also is a late process. X-ray reveals a few, dark fine streaks along the course of the muscle, a few hours later, however, the gas collects in small pockets and gives a typical mottled appearance to the film. The blood shows no great increase in the leucocytes, but indicates a severe anemia. Blood cultures are only rarely positive (5). If such cases are untreated, the infection runs its cours, and ends fatally in 12-24 hours after the date of injury.

(B) THE FULMINATING TYPE: In the common type the rapidity of the spread was striking; in this type the speed of the sequence of events is even more dramatic. This is especially apt to follow conditions where shock and blood loss are marked, and it is this symptom complex of shock, hemorrhage, and exhaustion, associated with the anaerobic infection, that combines to produce these cases. Such patients when first seen are usually cold, pale, restless, and usually vomiting. The pulse is often imperceptible at the wrist and the systolic blood pressure is around 50 mm of mercury. Locally the wound presents a very similar appearance to that described above, but extensive gas formation may occur within a short time. When in this state the patient cannot stand much surgical interference, and death oftentimes takes place in 10-24 hours, or less, after the initial injury.

(C) THE DELAYED TYPE: Here both the local and general resisting powers of the individual have succeeded up to a point and the latent infection is limited to the surface of the wound. At a variable time interval, and oftentimes following some new stimulus such as injury or operation, constitutional symptoms appear, and the disease runs a typical course. Krymov has emphasized this property of latency, and even claims that he has found cases in which such latency existed for as much as 15 years after the initial infection and before signs or symptoms developed (58).

DIAGNOSIS

The diagnosis of gas bacillus infections must depend not only upon one's ability to judge clinical findings, but on the laboratory findings as well. The points in the clinical picture which are of most importance in making the diagnosis are:

(1) pain, which is the most common symptom
(2) rapid pulse, which is the most common sign
(3) swelling
(4) local discoloration
(5) crepitus
(6) the characteristic odor

As regards laboratory aids, those of undoubted diagnostic importance are:

(1) bacteriological findings
(2) the roentgenogram
(3) various animal injection tests

Nearly all who have written on this subject agree that pain of severe degree is probably the earliest ymptom found in such cases. Acoompanying this pain is the swelling, which is usually of a firm type, without much fluctuation, until necrosis is well established. Probably one of the most significant of the early signs is the elevation in thepulse rate. While this is, of course, not diagnostic of gas infections alone, yet it is one of the earliest and most definite signs. As a rule it is way out of proportion to the elevation of temperature. The color changes have been described in detail. Crepitus is one of the signs looked for most frequently and considered so characteristic. It must be remembered, however, that this is a comparatively late finding. The odor is

said to be characteristic , however it is interesting to note the various attempts to describe it in the different accounts. It is putrefactive, offensive, and "mousey," however he who attempts to diagnose the condition on the odor alone will come to grief.

Bacteriological findings are oftentimes of value to the clinician. A smear and culture of the wound should be taken in all doubtful cases. If the smear shows organisms of suspicious nature to one familiar with the examination of such smears, Ghormley advocates that the institution of treatment is justified (38). The report of the culture will necessarily be delayed and one should not wait to receive it before beginning treatment when gas gangrene is suspected. It is, however, of value in fonfirming latent infections. Reeves has advocated a capsule stain as the most reliable single laboratory procedure, claiming that B. Welchi is the only pathological anaerobe with a capsule (83).

Schwartz, in 1915, called attention to the appearance of the gas in the tissues upon the roentgenogram, and advocated this procedure as an aid in making an early diagnosis (56). Since that time, many investigators have emphasized this extremely valuable diagnostic aid (63, 91, --19, 75).

Various animal injection procedures have been proposed, but none have come into wide favor as yet. Jennings, in 1923, advocated injection of suspected matter into the ear vein of the rabbit. The animal was then killed by a blow on the head, and incubated for 12

hours. With the presence of B Welchi.the carcass was found to be greatly emphysematous and the organism could be recovered from the organs, especially the liver. This test is rarely necessary, however (50). Nerb, in 1927, advanced a plan for injecting suspected material into the liver of the Guinea Pig, taking care to traumatize the liver in the injection. This animal was then killed, incubated for 12 hours, and examined for similar findings (76). Reeves has thrown some doubt upon the accuracy of these two tests, by demonstrating that in each case similar results can be obtained by use of sterile saline injections. (83).

TREATMENT

The treatment of gas gangrene of the extremities resolves itself into an early recognition of the condition and the immediate institution of all prophylactic and active therapeutic measures available. The ever mounting number of cases of this condition seen in civil life may be attributed, at least in part, to the hesitancy to utilize proper measures, procrastination, or to sheer ignorance of the morbid prognosis of all crushing injuries of the extremities.

As early as 1893, Fraenkel advised incising the parts freely so that air could reach the diseased tissues, and also stated that the application of an oxidizing agent such as $KMnO_4$ or H_2O_2 might be of value. This statement was made only two years after Welch announced the discovery of his organism (32). Mann, in 1894, reported a case treated with long, free incisions and hot $HgCl_2$ packs (67). Prior to the World War the treatment of this condition tended to be radical, and it became generally held that early amputation was always indicated. In 1912, Cramp advocated more conservative measures, and reported several cases treated according to Fraenkel's original recommendations, with encouraging results (17). Local excision of diseased tissue was practiced occasionally in civil surgery, but it was not until the World War that the value of debridement, as we know it today, was fully appreciated. During the Great War the use of specific serum, both prophylactically and therapeuticly, was introduced.

(A) PROPHYLAXIS

The prophylactic treatment of gas bacillus infections becomes largely an evaluation as to what wounds are apt to give rise to the infection. In all injuries in which there has been much maceration or crushing of tissue, one should be on his guard for the possibility of anaerobic infection. If any suspicion of gas gangrene arises, there should be prompt debridgement of the wound. Although some men have gone so far as to recommend immediate amputation as a means of prophylaxis, the consensus of opinion seems to be against this radical procedure (56).

Following the serologic work of Leclainche and Vallee (62), Sacqupee (87), Weinberg (108), Bull and Pritchett (13), and others, the use of this serum as a means of prophylaxis was intensively investigated. In 1917, Duval and Vaucher reported 50 cases in which a combination antiperfringens, antioedematiens, and antivibrionary serum prepared by Weinberg and Sequin was injected prophylactically. In none of the patients did gas gangrene develop, although all were of the most severely wounded type (24).

In 1918, the same authors reported 281 cases in which severely wounded men were injected with serum from the Pasteur Institute, a pooled serum similar to the one of Weinberg. Here, 6.4% developed gas gangrene with ten deaths or a mortality rate of 3.5%, which was lower than that which those authors call the usual mortality rate from gas gangrene in the severely wounded (16%).

They expressed themselves as being enthusiastic over this measure (25).

Mairesse and Regnier, in the same year, reported that of 1,016 wounded men examined bacteriologically, 297 showed gas bacillus contamination. These were given prophylactic injections as indicated by the bacteriologic report, and in 10% of the cases, gas gangrene developed (66). Many other investigators reported cases so treated during the latter years of the war, and in most cases expressed themselves as being greatly satisfied with the results (62, 26, 4, 49, 103, 86, 64, 2).

In the Spring of 1918, the British made a considerable test of sero-therapy, using a weak, polyvalent serum containing antitoxin against the three gas bacilli and B. tetani. Prophylactic doses were given to 15,000 soldiers; 15,000 controls were selected, and records were kept of those developing gangrene in both groups. When all of the results were in, a careful review showed that there was no significant difference in the incidence rate. Apparently, however, the investigators were impressed, for they laid the failure to secure positive results to the weakness of the serum that was then available (103).

Early in the spring of the same year, bacteriologists who had been working in France on the Gas Bacillus problem were sent back to the United States to start the manufacture, on a large scale, of an antigangrenous serum. For several reasons the manufacture

progressed slowly, but, in the fall of 1918, about 5,000 doses of serum reached the central laboratories of the A.E.F., and precautions were made to test it on the wounded. In all about 2,500 were treated and 2,500 controls were selected. On the whole the results were encouraging, and it is believed that if the Armistice had not interrupted the progress of the test, a very favorable report might have been finally rendered, which would have dictated the employment, as a routine measure, of the anti-gas serum in the future. (103).

In November, 1917, the Third Interallied Contress for the Study of War Wounds reported that the serum seemed to have given favorable results as a preventative, and one year later, the same conservative body reported that preventive serotherapy in the French Army had reduced the frequency of gas gangrene. (90).

Penfold and Tolhurst, in 1937, reported the results of their work on Guinea Pigs, in which they used alum precipitated suspensions of formol toxins of B Welchi as an immunizing agent. They demonstrated both active and passive immunitey, and seem to be very enthusiastic over the future (79.).

Thus we see that the use of serum as a prophylactic agent has been widely urged. Although it is not as effective in the prevention of gas gangrene as tetanus antitoxin is in the prevention of tetanus, it is felt by all investigators that there is sufficient evidence of its value to justify its use in the prophy-

lactic treatment of badly contaminated wounds. Five thousand units is usually considered as a prophylactic dose, but no hard and fast rules can be laid down covering its use, as each case must be considered by itself. It has been stated that the average morbidity of gas gangrene among those in the World War who had received prophylactic injections was around 0.6%, while among those who had not received the injections, the morbidity was around 2-3%.

The prophylactic dose of polyvalent gas gangrene anti-toxin is now prepared in conjunction with tetanus antitoxin for commercial sale. But for its cost it should be given in all street accident cases. For the private patient the cost can not be of any importance if the likehood of complication by this dread disease may be reduced. In addition to sera, it is of importance to direct attention to certain other means of preventing the development of this condition. Shock must be energetically combated. Whenever possible either local, spinal, or nitrous oxide anesthesia should be used as the anesthetic, as ether and chloroform tend to the production of acidosis and so favor the production of gas infection. Blood transfusion has proven to be a valuable aid in combating the anemia. Finally, in cases where anoxemia of the tissues may be predicated on the basis of a preexisting arterial disease, the use of a tourniquet, even though it may facilitate the performance of an operation, should be contraindicated astending

to further impair the nutrition of the tissues.

(B) ACTIVE TREATMENT:

(1) SURGERY: The surgical treatment of wounds in which gas infection is present was explicitly outlined by the Medical Corp of the United States Army just before the battle of Chateau-Thierry. This outline in the main applies to civil cases as well as to military ones.

a - Operate as early as the diagnosis is made. This has been emphasized by Kummell (59), Schmid (93), Kausch (52), Seefisch (94), and Schoessmann (92).

b - In cases in the extremities, avoid the use of a tourniquet.

c - Make incisions longitudinally, and half again as long as thought necessary in both skin and fascia.

d - Go between muscles rather than through or across them. Most surgeons have come to this conclusion (46, 114, 33).

e - Excise all discolored, noncontractile muscle, and all other infected tissue as well as any foreign bodies. By the removal of an entire infected muscle or group of muscles, the spread of infection may be stopped, and amputation may be avoided. Frankau (33) advocated this very important procedure, as did Lardennois (60), Weinberg (109), and Schmid (93).

f - Leave the wound wide open. Dress the wound with gause, laid in, not packed in.

g - Carrol tubes should be placed deep in the wound for irrigation

only if it is sure that they will be properly taken care of.

h - Parts that have inadequate blood supply, or those in which gangrene is already present, should be amputated at once.

j - When amputation is necessary, disarticulation should be done when feasible. If this is not possible, the guillotine amputation is the operation of choice.

(2) SEROTHERAPY:

During the later years of the war in France, individual sera were prepared against various organisms which had been found in gas infections. In 1917, Bull and Pritchett demonstrated for the first time the presence of a true exotoxin in B Welchi cultures. Using this toxin, they then developed an antitoxin in rabbits, which they found to be curative as well as preventive in pigeons. By giving this serum prophylactically to the laboratory animals, and then comparing the sensitivity, with controls, to the intrvenous injection of the toxin, they were able to demonstrate a passive immunity conferred as a result of the antitoxin. They concluded that the antitoxin was of definite value in animals, and that it should be attempted in man (113, 14). Further investigation, however, revealed that this, as well as other individual sera, was a failure, and the reason was not very difficult to determine. As pointed out by Weinberg and Sequin (111), Selter (95), and Nevin (77), the antisera prepared for one organism was powerless to combat the growth of the other organisms which were

invariably found in gas infections.

Following this, polyvalent sera were proposed by Weinberg and Sequin (111), Leclainche and Vallee (62), and Vincent and Stodel (105). Although the polyvalent serum did not seem to be specific in the cure of the disease, a prompt dropping in the mortality was noted. Weinberg and Sequin reported nineteen cures in thirty cases (111). Bazy, reporting on the results of two years investigation into serotherapy, stated that encouraging results were being obtained, but did not give his mortality rate (4). Favorable results were also reported by Sacquepee (90, 88), Weinberg (108, 109, 110), and Leclainche and Vallee (62). Rouvillois, et al, reported in 1918 the results of one year's investigation with polyvalent serum. They compared cases treated with serum plus surgery with others treated with surgery alone, and stated that the addition of the serum reduced their mortality by 50% (86). Sacquepee and Vezeau de Lavergne presented experimental evidence favoring the use of serum. They were able to reproduce the infection by the introduction of macerated infected muscle tissue into the leg of Guinea Pigs. They then demonstrated that the addition of serum either prevented development of the disease or greatly alleviated it (89). Van Beuren, in 1919, stated that while improvement in war results were being obtained by surgery alone even before the introduction of serotherapy, the use of serum had undoubtedly been of definite aid (103).

In this country until 1928, a polyvalent serum was not obtainable, and the results obtained from the use of the simple perfringens serum were for the most part unsatisfactory (72). Where the polyvalent serum has been used, however, the results have been eminently satisfactory (61, 16, 65).

At the present time several commercial brands are on the market, but it is essential that they contain antibodies against B Welchi, Vibrion Septique, B Oedematiens; the others do not seem to be of such significance (72). The antitoxin should be given in rather massive doses, since the degree of toxemia and local tissue reaction is great. The use of 50,000 to 100,000 units is advised (19). It may be given intra-venously or intra-muscularly, as well as applied directly to the wound. As with its prophylactic use, no hard and fast rules may be laid down governing its use, but each case must determine this for itself; the important thing seems to be giving the serum in sufficiently large doses.

(3) X-RAY RADIATION

In 1933, J F Kelly reported six cases of gas infection of the extremities treated with the accepted surgical and serologic measures plus the use of small doses of X-ray, all of which recovered. He stated at that time that he was at a loss to explain the apparent beneficial results but strongly recommended the further investigation of its value by other men (55). This is the

recorded instance of the use of X-ray in the treatment of this condition, although Desjardius, in 1931, had published a review of the use of the X-ray in many other inflammatory conditions (23).

One year later (1934), Faust reviewed 7 cases treated with slightly stronger doses of X-ray with good results. He stated that as a possible explanation of the mode of action, that radiation of live tissue was known to liberate H202, and that this agent might be the effective agent in overcoming the infection. He also stated that the X-ray was of marked value in the condition, and should be further investigated (29, 30).

In 1936, Kelly again reviewed 40 cases of his own and of others, in which X-ray had been used. He stated at this time that the mortality for the entire series was 8.9%, a marked reduction from that reported in any series up to that time. As regards technic, he recommended that the readiation be given morning and evening over a period of at least three days and of sufficient voltage to insure penetration of the involved tissue: from 90-100 kilovolts on an extremity, 1 mm aluminum filter, from 130-160 kilovolts on the trunk with increased filtration; about 100 roentgens per treatment over each area (56, 57).

While still comparatively new, this addition to our armamentarium is rapidly becoming recognized as one of our most efficient weapons in combating this infection.

(4) OXIDIZING AGENTS

As stated above, Fraenkel advocated the use of H202 as long ago as 1893, just one year after the discovery of the organism by Welch. Since that time many investigators have employed this and other oxidizing agents in the treatment of active gas bacillus infections. The rationale has been to combat the organisms on a biological basis, in the hope of oxygenating the tissues and of thus rendering them unsuitable for the growth of anaerobic bacteria.

During the World War, Seefisch (94), Bocker (7), and Borchers (10) advised the use of free Oxygen by insufflation as well as by direct injection into the infected area. Borchers, however, stressed the dangers of air embolism in this procedure, and reported five fatalities because of this complication.

From time to time, KMnO4 has also been advanced as a means of attack, working along the same line as the use of Oxygen and H202. In general, however, the results seem to have been no better than those obtained with the usual measures (100). Indeed Delbet showed experimentally that the gas bacillus grew better on muscle tissue previously treated with H202 than on muscles not so treated (21). Though of auxillary value in the treatment of the disease, it can be said at the present time that no one or combination of these agents can be considered as invaluable in a case of impending or progressing gangrene (72). What the future holds through the

further investigation of their value, can not be foretold at this time.

(5) NON-SPECIFIC ANTISEPTICS

In the past, practically every known antiseptic has been advocated in the chemotherapy of this disease. Iodine (7), iodoform, nitrate of silver, hypochloride of soda (11a), Gentian Violet (6), carbolic acid (48), hypertonic salt solution (48), formalin (74), alcohol (74), Mercurochrome (3), and soap have all been employed. All have been disappointing, either because it was found that when strong enough to be really bacteriocidal these agents caused death of tissue and so predisposed to spread of the infection, or when weak enough to be non-injurious to the tissues they were practically useless as antibacterial agenst. Thereupon the discontinuous use of antiseptic solutions such as Dakin's solution was suggested but with similarly unsatisfactory results. It was felt that though this solution was useful as a bacteriocide and as a detergent, it was disadvantageous in that, at the same time, it flushed away the protective antibodies and leucocytes.

As a result of Taylor's demonstration of the bacteriocidal effect in vitro of a 1% solution of quinine sulfate on the gas bacillus (100), Pilcher suggested a quinine mixture which was employed by him with considerable satisfaction (81), but again it does not seem to have received general approval. Delbet, because

of its positive chemotaxis for leucocytes, recommended a solution of 1.21% magnesium sulfate (21). Phototherapy, heliotherapy, and thermotherapy have all been used but with the same indifferent success.

Bohlman, in 1937, reported three cases treated with Sulfanilamide. Twenty to seventy-five grains were given daily by mouth. All three cases recovered, and he is quite enthusiastic over the possibilities (8). This agent is still too new to have been properly investigated, but needs further study in the treatment of this condition.

PROGNOSIS

The prognosis of any one case of gas gangrene depends largely upon the rapidity with which treatment is instituted. Mortality figures quoted by different investigators have varied rather widely. This is due in part at least to the development of an increasingly more efficacious attack upon the condition, both prophylactically and therapeutically, especially during the World War.

Kummel, in 1915, stated that in his war experience, the mortality was around 32%. He contrasted this figure with what he claimed was the average mortality during times of peace (80-85%). He was not, however, able to satisfactorily explain this (59). Bocker claimed that the war figure should be closer to 80% (7), while Lardennois analyzed 500 cases during 1915-1916 and stated that the mortality was only 15% (60). Gross estimated that treatment should be given early by pointing out that a delay in beginning treatment of 12 hours would increase the mortality from 11% to 56%. He obtained this impression by studying 3,300 wounded men (43). Other figures given from a study of war injuries are Ivens, 10% (48); Gross, 42% (142); Van Beuren, 32% (103); Duval and Vaucher, 16% (2 5); Mairesse, 10% (66).

The mortality from this condition was estimated by Zindel to be from 12-50% in military practice and from 70-90% in civil practice (40). Loehr quotes the Medical Research Committee as having placed the mortality at from 20-50% for the Allies and

from 30-60% for the Central Powers (64).

As regards studies of civil series, Weintrob and Messeloff reviewed 85 cases with a mortality of 45.9% occurring before 1927 (110). Manson, after an exhaustive search, stated (1932) that the average mortality in American Civil practice was around 40% (68). Millar, in 1932, reviewed 607 cases occurring after 1883. These constituted all of the cases that he could obtain from a study of the literature, and, of course, represented all forms of treatment. Of this entire series, 50.3% died. He also states that the American Expeditionary Force in France had a death rate according to the Surgeon General's Office of 48.5%, and that the official British Expeditionary Force report gives a mortality of 20-50% (73).

Stone and Holsinger, in 1934, reviewed 67 cases occurring from 1921 to 1933 at the Virginia State Hospital with a mortality of 32.4% (99). Kelly, reporting his series treated with the aid of X-ray, gives a mortality of 8.9%, an amazingly low figure. (56).

BIBLIOGRAPHY

(1) Albrecht, A - The Treatment of Gaseous Gangrene - Beil Klin Wchnschr - 29:940-1916-Abstracted in International Abstract of Surgery - 24:520 - 1917

(2) Angerer, H - The Treatment of Gas Gangrene - Arch f klin chir - 178:179-1933-Abstracted in International Abstract of Surgery - 62:108 - 1936.

(3) Arnulf, G & Frieh, P - Intra-Arterial Injections of Antiseptics - Presse med Par - 44:629 - 1936 - Abstracted in International Abstract of Surgery - 63:276 - 1936

(4) Bazy, L - Remarks on the Serotherapy of Gas Gangrene - Bull et men Soc de chir de Par - 44: 1213 - 1918 - International Abstract of Surgery - 27:493 - 1918

(5) Binghold, K - The Clinical Forms of Gas Bacillus Infection - Deutsche med Wchnschr - 2:1727, 1767, 1800, 1887 - 1935 - International Abstract of Surgery - 62:473 - 1936

(6) Blaustein, N - The use of Gentian Violet in the Treatment of Gas Gangrene - Medical Record - 143: 319 * 1936

(7) Bocker, W -The Treatment of Gaseous Phlegmon in the Field - med klin Beil - 11:329 - 1915 - Interantional Abstract of Surgery 21:79 - 1915

(8) Bohlman, H R - Gas Gangrene Treated with Sulfanilamide - J A M A - 109:254 - 1937

(9) Boland, F K - Gas Gangrene in Compound Fractures - Ann Surgery - 90:603 - 1929

(10) Borchers, E - The Use of Oxygen in the Treatment of Gas Gangrene - Muenchen med Wchnschr - 62:1338 - 1915 - International Abstract of Surgery - 22:268 - 1916

(11) Brichner, W M & Milch H - Gas Gangrene Infections - Inter Clinics - 6:226 - 1926

(12) Bull, C G - An Antitoxin for B Welchi - J of Exp Med -26:603 - 1917

(13) Bull, C G & Pritchett, I W - Toxin and Antitoxin of B Welchi - J of Exp Med - 26:119 - 1917

(14) Bull, C G & Pritchett, I W - Toxins of Various Strains of B Welchi - J Exp Med - 26:867 - 1917

(15) Bullock, W E & Cramer, W - On the Mechanisms of Bacterial Infection - Imperial Cancer Research Fund - Report #6 - 1919 - London, Taylor and Francis

(16) Burnett, W E - The Serum Treatement of Gas Gangrene - Penn Med J - 36:174 - 1932

(17) Cramp, W C - A Consideration of Gas Bacillus Infection - Ann Surgery - 56:544 - 1912

(18) Davis, G G - Gas Bacillus Infection - Industrial Med - 5:234 - 1936

(19) Davis, GG - Roentgen Ray in the Diagnosis of Gas Gangrene - S G & O - 22:635 - 1916

(20) Dawson, J W - The Healing of Incisional Wounds - J Path and Bact - 13:174 - 1909

(21) Delbet, P - The Use of H202 in the treatment of Gas Gangrene - Comptes Rendus de l'Academie des Sciences - 161:268 - 1915 - quoted by 72

(22) Delbet, P - The Treatment of Gas Gangrene - Bull de la societe de chir - 41:1524 - 1915 - quoted by 72

(23) Desjardius, A U - Radiotherapy for Inflammatory Conditions - JA M A - 96:401 - 1931

(24) Duval, P & Vaucher, E - Antitoxic Serum for Gas Gangrene - J A M A - 71:991 - 1915

(25) Duval, P & Vaucher, E - Antigangrenous Serotherapy - bull et eme soc de chir de Par - 44:1535 - 1918 - International Abstract of Surgery - 29:106 - 1919.

(26) Duval, P & Vaucher, E - Antigangrenous Serotherapy - bull et mem soc de chir de Par - 44:1187 - 1918 - International Abstract of Surgery - 27:493 - 1918

(27) Emrys-Roberts, E & Cowell, E M - Gas Gangrene of Muscle - J Path and Bact - 21:473 - 1917

(28) Fasiani, G M - On the Asserted Transformation of Anaerobic Bacilli of Gas Gangrene - Sperimentale - 72:459 - 1919 - International Abstract of Surgery - 29:287 - 1919

(29) Faust, J J - Report on the X-ray Treatment of Gas Gangrene Cases - Radiology - 22:105 - 1934

(30) Faust, J J - Radiation Therapy of Gas Gangrene Infections Ill Med J - 66-547 - 1934

(31) Finesilver, E M - Gas Bacillus Infection - J Med Soc New York - 31:194 - 1934

(32) Fraenkel, E - Emphysematous Phlegmon - Centralbl f Bakterial

u Parasitenk - Hamburg and Leipzig - 1893 - quoted by #67

(33) Frankau, C H S & Drummond, H - The Successful Early Treatment of Gas Gangrene - Brit Med J - 1:729 - 1917

(34) Fraser, J & Bates, R - Hypochlorous Acid in the Treatment of Gas Gangrene - Brit Med J - 1:83 - 1916

(35) Freund, H - Experiences with Gas Gangrene in War Surgery - Beitr z klin chir - 98:447 - 1916 - International Abstract of Surgery - 23:493 - 1916

(36) Gage, I M - Experimental Production of Gas Gangrene - Proc soc Exp Biol and Med - 29:914 - 1932

(37) Gemmill, W F * Emphysematous Gangrene with Report of cases - S G & O - 33:650 - 1924

(38) Ghormley, R K - Diagnosis and Treatment of Gas Gangrene - J Bone and Joint Surgery - 17:907 - 1935

(39) Graham, J C, Stewart, S H, & Baldwin, J F - The Bacillus Aerogenes Capsulatus - Columbus Med J - 12:55 - 1893

(40) Grantham, S - A Clinical Study of the Welch Bacillus - J Mo State Med Assn - 32:273 - 1935

(41) Greene, J S - On the Presence of Air in the Veins as a Cause of Death - Amer J Amer Sciences - 47:38 - 1864

(42) Gross, G - Gaseous Gangrene - Bull de l'acadamy de med - 76: 586 - 1916 - International Abstract of Surgery - 24:616 - 1917

(43) Gross, G - 134 Cases of Gas Gangrene - bull et mem so c de chir de Par - 43:636 - 1917 - International Abstract of Surgery - 25:243 - 1917

(44) Gwyn, N B - Infection with Bacillus Aerogenes Capsulatus - Johns Hopkins Hosp Bull - 10:134 - 1889

(45) Hare, H A - Emphysematous Gangrene - Prog Med - 1899 - 4: 158

(46) Hartman, W L - The Treatment of Gas Bacillus Infection Am J Surg - 29:451 - 1915

(47) Henry, H - On the Composition of B Welchi Toxin - J Path and Bact - 26:497 - 1923

(48) Ivens, M H F - A Clinical Study of Anaerobic Wound Infections

Med Presse & Circ - 103:12 - 1917 - International Abstract of Surgery- 24:617 - 1917

(49) Ivens, M H F - Preventative and Curative Treatment of Gas Gangrene with Mixed Sera - Brit Med J - 2:425 - 1918

(50) Jennings, J E - Gas Bacillus Infections - New York Med J - 117:682 - 1923

(51) Jurgenson, H - Emphysematous Gangrene - Deutsches Archiv f klin med - 41:569 - 1887 - quoted by #113

(52) Kausch, H - Gas Phlegmon - Beitr z klin chir - 97:7 - 1915 - International Abstract of Surgery - 21:619 - 1915

(53) Keen, W W - A Contrast Between Surgery of the Civil War and of the Present War - N Y Med J - 101:817 - 1915

(54) Keen, W W - The Treatment of War Wounds - W B Saunders Co Phil and London - 1917

(55) Kelly, J F - The X-ray as an Aid in the Treatment of Gas Gangrene - Radiology - 20:296 - 1933

(56) Kelly, J F - The Present Status of the X-ray in the Treatment of Gas Gangrene - J A M A 107:1114 - 1936

(58) Krymov, A - Latent Gas Bacillus Infection - Nov chir arch - 28:300 - 1933 - International Abstract of Surgery - 58:364 - 1934

(59) Kummell, H - Wound Infection - Beitr z klin chir - 96: 421 - 1915 - International Abstract of Surgery - 21:417 - 1917

(60) Lardennois, G & Baumel, J - The Malignant Infection of War Wounds by Anaerobic Bacilli - Presse Med - 1:506 - 1916 - International Abstract of Surgery - 1917

(61) Larson, E R & Pulford, D S - Gas Gangrene of the Extremities - J A M A - 94:612 - 1930

(62) Leclainche, G & Vallee, E - Specific Serum Treatment of Wounds - Bull et mem soc de chir de Par - 42:1804 - 1916 - International Abstract of Surgery - 1917 - 24:44

(63) Ledoux-Lebard, R - The Radiological Diagnosis of Gas Gangrene - J de radiol et d'elect - 2:241 - 1916 - International Abstract of Surgery - 24:57 - 1917

(64) Loehr, W - Gas Gangrene - arch f klin chir - 179:312 - 1934 - International Abstract of Surgery - 62:108 - 1936

(65) MacKechnie, D M - The Use of H202 in the Treatment of Gas Gangrene - Lancet - 2:1332 - 1936

(66) Mairesse, I & Regnier, I - Serotherapy of Gangrene in War Wounds - Presse med - 26:461 - 1918 - International Abstract of Surgery- 28:152 1919

(67) Mann, A H - A Case of Aerogenes Capsulatus Infection with Emphysematous Gangrene - Ann Surg - 19:187 - 1894

(68) Manson, M - Anaerobic Bacilli in Chronic Ulcers - Arch Surg - 24:752 - 1932

(69) May, G - Three Case Reports of Air Found in the Vessels at Autopsy - Brit Med J - 1:603 - 1857

(70) May, G - Two Case Reports with Air Found in the Vessels after Death - Tran P th Soc of London - 9:154 - 1858

(71) McNee, J W & Dunn, J S - The Method of Spread of Gas Gangrene Brit Med J - 1:727 - 1917

(72) Milch, H - The Treatment of Gas Gangrene - Ann Surg - 93:1220 - 1931

(73) Millar, W M - Gas Gangrene in Civil Life - S G & O - 54:232 - 1932

(74) Morestin, H - The Use of Formalin in Wounds - Bull et mem soc de chir de Par - 41:740 - 1915 - International Abstract of Surgery - 21: 418 - 1915

(75) Morgan, J D & Vilandre, G - The Use of the X-ray in the Early Diagnosis of Gas Gangrene - Brit Med J - 1:8 - 1917

(76) Nerb, L - A Method for Identification of B Welchi - Surg Clinics of No Amer. - 7:1021 - 1927

(77) Nevin, M - Experimental Gas Gangrene - J of Infectious Diseases - 2:178 - 1919

(78) Pasteur, L - Bull Acad de med - 1:781 - 1877 - quoted by #67

(79) Penfold, W J & Tolhurst, J C - Formol Toxoids in Prophylaxis of Gas Gangrene - Med J of Australia - 1:983 - 1937

(80) Pettit, R T - Infections of War Wounds - J A M A - 73:1919 - 1919

(81) Pilcher, J - Treatment of Gas Gangrene - Ann Surg - 81: 206 - 1925

(82) Razzaboni, G - A Study of the Action of Certain Organs and Systems in Gas Gangrene - S G & O - 31:38 - 1920

(83) Reeves, J R - Infections with Gas Forming Bacilli - J A M A - 104:526 - 1935

(84) Reports to the Surgeon General - U S Medical Corp - 12:407

(85) Reports of the Medical Research Committee - Anaerobic Infections of Wounds - Series #39 - London - 1919

(86) Rouvillois, G - Treatment of Gas Gangrene by Antigangrenous Sera - Bull et mem soc de chir de Par - 62:1338 - 1918 - International Abstract of Surgery - 23:137: - 1916

(87) Sacquepee, E - Researches on Gas Gangrene of War Wounds - Presse med Par - 26:197 - 1918 - International Abstract of Surgery - 27:330 - 1918

(88) Sacquepee, E - Antitoxin Treatment of Gas Gangrene - J A M A - 70:554 - 1918 - (Paris Letter)

(89) Sacquepee, E & Lavergne, V - Gas Gangrene - Bull et mem soc de chir de Par - 42:1125 - 1918 - Internation Abstract of Surgery - 28:493 - 1919

(90) Sacquepee, E & Wright, R - Report of the Third Allied Surg Congress for the Study of War Wounds - Arch de med et Pharm mil - 69:18 - 1918 - International Abstract of Surgery - 27:330 - 1918

(91) Savill, A - X-ray Appearance of Gas Gangrene - Arch Radiol & Electrotherapy - 21:201 - 1916 - International Abstract of Surgery - 24: 614 - 1917

(92) Schloessmann, R - Open Dry Treatment of Gas Gangrene - Muenchen med Wchnschr - 62:1653 - 1915 - International Abstract of Surgery - 22:501 - 1916

(93) Schmid, H H - Treatment of Gas Gangrene - Wien klin Schnschr- 28:556 - 1915 - International Abstract of Surgery - 21:417 - 1915

(94) Schwartz, G - The Recognition of Gas Gangrene in the Roentgen Plate - Wien, klin. Wchnschr. - 28:92 - 1915 - International Abstract of Surgery - 21:79 - 1915

(95) Seefisch, G - Gas Phlegmon in the Field Deutsche med Wchnschr - 61:256 - 1915 - International Abstract of Surgery - 21:178 - 1915

(96) Selter, H - Etiology of Gas Gangrene - Deutsche med Wchnschr - 61:1189 - 1915 - International Abstract of Surgery - 22:189 - 1916

(97) Sieur, I & Mercier, R - Gas Gangrene in 1918 - Bull - de l'Acad de med - 80:394 - 1918 - abstracted in J A M A - 71:2181 - 1918

(98) Simonds, R - Studies with B Welchi - Rockefellow Institute for Medical Research - Monograph 5 - 1915

(99) Stewart, J C - Anaerobic Cellulitis - J A M A - 45:528 - 1905

(100) Stone, C S & Holsinger, H B - Diagnosis and Treatment of Gas Gangrene - Virg Med Monthly - 61:200 - 1934

(101) Taylor, J L - Gas Bacillus Infections - Lancet - 45:548 & 1925

(102) Taylor, J L - Gas Bacillus Infections - J Path and Bact - 13:174 - 1909

(103) Touraine, A - Gas Gangrene Following Injections of Antiseptics - Presse med Par - 44:629 - 1936 - International Abstract of Surgery - 63:276 - 1936

(104) Van Beuren, F T V - The Treatment of Gas Gangrene - J A M A 73:239 - 1919

(105) Van Gehuchten, P - Organs of Internal Secretion in Experimentat Gas Gangrene - Ann de l'Acad Pasteur - 35:396 - 1921 - quoted by #43

(106) Vincent, H - Prophylaxis and Therapy of Gas Gangrene - Inter Clinics - 4:138 - 1925

(107) Wallace, C - Color Changes in Gas Gangrene - Brit Med J - 1:725 - 1917

(108) Warthen, H J - Gas Bacillus Infections - Virg Med Mon - 62:276 - 1935

(109) Weinberg, M - Bacteriological and Experimental Researches on Gas Gangrene - Proc Roy Soc Med - 9:119 - 1916

(110) Weinberg, M - Bacteriological and Experimental Researches on Gas Gangrene - Lancet - 190:622 - 1916

(111) Weintrob, M & Messeloff, C R - Gas Gangrene in Civil Practice - Amer J Med Sciences - 174:801 - 1927

(112) Weinberg, M & Sequin, G - Gas Gangrene - Mason et Cie - Paris - 1918 - quoted by #72

(113) Welch, W H - Morbid Conditions Caused by B Welchi - Bull J Hopkins Hosp - 11:185 - 1900

(114) Welch, W H & Flexner, S - Observations Concerning the Bacillus Aerogenes Capsulatus - J Exp Med - 1:5 - 1896

(115) Welch, W H & Nuttal, H F - A Gas Producing Organism Capable of Rapid Development in the Blood Vessels after Death - Bull J Hopkins Hosp - 3:81 - 1892